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Relationship between Preoperative Frailty and Postoperative Outcomes after LVAD Implantation

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By

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Abstract

Background: Frailty is common in many patients with advanced heart failure, including those who undergo left ventricular assist device (LVAD) implantation. Frailty has been associated with worse outcomes after other cardiac surgeries; however, little is known about the effect of frailty on postoperative outcomes after LVAD implant.

Purpose: The purpose of this project was to evaluate whether preoperative frailty [as determined by either short physical performance battery (SPPB) score ≤ 7/12 or 6-minute walk test (6-MWT) <200 meters] is associated with poorer postoperative outcomes after LVAD implantation than non-frailty in adults with advanced heart failure.

Setting and Sample: This project was conducted at UK Chandler Hospital, a 945-bed, academic medical center. 120 adult advanced heart failure patients who had an LVAD implanted at UK Chandler Hospital between May 2015 and April 2020 were included in the sample.

Design: This project was a descriptive study employing retrospective and prospective chart review.

Methods: Data was collected through chart review from LVAD patients with documented preoperative 6-MWT and SPPB scores. Patients were considered frail if they had a 6-MWT <200 m or SPPB score ≤ 7/12. Postoperative outcomes of hospital and ICU length of stay (LOS), time mechanically ventilated, placement of tracheostomy, discharge disposition, inpatient and one-year mortality, hospital readmissions at 30 and 90 days, and change in pre- and postoperative quality of life scores (QOL) were compared between frail and non-frail patients. Demographic and health data were collected and compared between frail and non-frail groups. Data was analyzed using SPSS software with the guidance of a university statistician.

Results: 41.1% of patients (n=46) had a SPPB score ≤ 7/12 and 53.3% of patients (n=64) had 6-MWT < 200 meters. When SPPB ≤ 7/12 was used to determine, frailty was associated with increased 1- year mortality (33.3 vs 15.6%, p=0.030), length of stay (LOS) (31 vs 18.5 days, p<0.001), ICU LOS (15 vs 9.5 days, p<0.001) time mechanically ventilated (81 vs 22.75 h, p <0.001), tracheostomy placement (31.1% vs 4.6%, p<0.001), and discharge to inpatient facility rather than home (55.0% vs 16.7%, p <0.001). When 6-MWT < 200m was used to determine frailty, frailty was associated with increased 1-year mortality (31.3 vs 13.2%, p=0.021), LOS (24 vs 19 days, p=0.021), time mechanically ventilated (71.25 vs 22.0 h, p <0.001), tracheostomy placement (23.8% vs 5.5%, p=0.006), and discharge to inpatient facility rather than home (47.4% vs 11.8%, p <0.001). ICU LOS was also longer (13 vs 10 days) for frail patients according to this measure but did not reach statistical significance (p=0.059). After adjusting for age, gender, BMI and other comorbidities, frailty defined by SPPB ≤ 7/12 was a significant predictor of increased ICU and hospital LOS, time mechanically ventilated, tracheostomy placement and discharge to inpatient facility, whereas 6-MWT < 200m was not a significant predictor in logistic regression models. No significant difference was found in inpatient mortality, 30 and 90-day readmission rates, or change in pre-and postoperative QOL scores for either frailty indicator.

Conclusion: Preoperative frailty is associated with worse postoperative outcomes, particularly, increased 1-year mortality, hospital and ICU LOS, time mechanically ventilated, tracheostomy placement, and discharge to an inpatient facility other than home after LVAD implant. Preoperative frailty assessment, should therefore, be completed on all patients prior to implantation, as the results can be used to help identify which patients may be less likely to benefit from this therapy or who may require more resources postoperatively. Based on this study's analysis, SPPB is likely a better measure of frailty than 6-MWT in predicting negative outcomes.

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Relationship between Preoperative Frailty & Postoperative Outcomes after LVAD Implantation

Background and Significance

Introduction/ Problem Identification

Frailty, which is characterized by increased physiological vulnerability, reduced resilience to stressors, and progressive loss of physiological function (Tse et al., 2018), is common in many patients with advanced heart failure, including those who undergo left ventricular assist device (LVAD) surgical implantation. Frailty has been shown to worsen patient outcomes after other types of invasive cardiac procedures and surgery (Bergquist et al., 2018); however, little is known about the effect of frailty on postoperative outcomes after LVAD implant, as few studies have been conducted examining the extent to which frailty increases the likelihood of adverse outcomes in this population.

Context, Scope, and Consequences of the Problem

Frailty has an estimated prevalence of 28% among adult patients with advanced heart failure (Joyce, 2016). Patients with heart failure and left ventricular dysfunction requiring LVAD implantation often have reduced exercise tolerance, cachexia, and a variety of comorbidities which may increase their risk for frailty. In fact, approximately 60% of patients undergoing LVAD implantation patient were found to be frail preoperatively (Joyce, 2016). Frailty may put patients at increased risk for complications post-implant. Large multicenter research studies and systematic reviews have demonstrated an association between frailty and worse postoperative outcomes including increased mortality and length of stay, prolonged mechanical ventilation, and complications such as bleeding and renal failure after other cardiac surgeries such as coronary artery bypass surgery or mitral and atrial valve surgeries (Abdullahi et al., 2017; Bäck et al. 2019; & Bergquist et al., 2018). As LVAD implantation, however, is designed to increase cardiac output and reverse symptoms of heart failure, it is unclear if preoperative frailty will influence postoperative outcomes in the same manner as in other cardiac surgeries.

Currently, however, few studies have specifically assessed the effect of preoperative frailty on postoperative outcomes after LVAD implantation. Preliminary studies have demonstrated worse outcomes for frail patients after LVAD surgery, including increased time to extubation, hospital length of stay, and long-term mortality (Joseph et al., 2016; Tse et al., 2018). Most of these studies assessed frailty using Fried scores or hand grip strength. At University of Kentucky (UK) Healthcare, however, frailty is assessed using different tools: SPPB and 6-MWT. Although both the SPPB and 6-MWT are validated tools frequently used to assess frailty in patients with advanced heart failure (Llopis et al., 2019 & Pandey et al., 2019), these particular tools have been minimally used in studies evaluating the effect of pre-operative frailty on post-operative outcomes after LVAD implantation. There was a need for additional research examining the effect of preoperative frailty on postoperative outcomes after LVAD implantation, specifically using 6-MWT and SPPB to assess frailty.

Purpose & Objectives

Therefore, a retrospective chart review was conducted to assess whether preoperative frailty (as determined by either SPPB ≤ 7/12 or 6-MWT <200 meters) is associated with poorer postoperative outcomes after LVAD implantation in adult patient with advanced heart failure.

Primary project objectives were to:

1) Assess whether preoperative frailty as measured by 6-MWT <200 meters is associated with the following poorer postoperative outcomes than non-frailty: 1) increased inpatient and one-year mortality, 2) increased hospital and ICU LOS, 3) increased time on mechanical ventilation, 4) increased frequency of tracheostomy placement, 5) less discharges home, 6) increased hospital readmissions at 30 and 90 days after discharge, and 7) less improvement between pre- and postoperative in QOL scores
2) Assess whether preoperative frailty as measured SPPB score ≤ 7/12 meters is associated with the following poorer postoperative outcomes than non-frailty: 1) increased inpatient and one-year mortality, 2) increased hospital and ICU LOS, 3) increased time on mechanical ventilation, 4) increased frequency of tracheostomy placement, 5) less discharges home, 6) increased hospital readmissions at 30 and 90 days after discharge, and 7) less improvement between pre- and postoperative in QOL scores

Additional project objectives were to:

1) Describe population sample using the following demographic and health data: Gender, race, age, Ejection fraction, New York Heart Failure (NYHF) Class/ American Heart Association (AHA) stage, BMI, Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profile score, cardiac index, presence of comorbid conditions (DM, HTN, CKD, COPD, RV dysfunction, & pulmonary hypertension), type of LVAD implanted, ischemic/non-ischemic cardiomyopathy, presence of prior sternotomy
2) Determine whether any demographic or health variables differ significantly between frail and non-frail groups
3) Determine if 6-MWT <200 meters or SPPB score ≤ 7/12 if a stronger predictor of negative postoperative outcomes
4) Determine whether demographic or health-related variable were more significant predictors of negative postoperative outcomes than pre-operative frailty
5) Compare patients' pre- and postoperative 6-MWTs and determine whether postoperative 6-MWT was a more significant predictor of negative outcomes than preoperative 6-MWT

Theoretical Framework

The theoretical framework selected to guide this project was *The Iowa Model of Evidence Based Practice to Promote Quality Care,* which was developed by Marita Titler and her colleagues (2001) at the University of Iowa and revised in 2017 by the Iowa Model Collaborative (Buckwalter et al., 2017. Appendix A). The Iowa Model outlines a multistep framework that nurses and clinicians can use to implement evidence-based practice (EBP). Under this model, clinicians identify a triggering issue that might warrant practice change, develop a related clinical question or project purpose, determine if the issue is a truly a priority at their institution, and assemble a team to review literature and gather data concerning the project/ question. At this point, the team must determine whether there is sufficient evidence to warrant a practice change. If there is not, the Iowa Model suggests that the team consider conducting additional research. Once evidence is sufficient to warrant change, the team then designs, pilots, and evaluates a practice change. If deemed appropriate, this change is adopted into long-term practice and results of the EBP change are disseminated to others.

In line with the Iowa Model, a triggering issue—the potential for adverse outcomes post-LVAD implantation due to preoperative frailty—was identified. This issue is of value at UK Healthcare, as patient outcomes measures are closely tracked after LVAD placement to improve upon care. Current evidence on the effect of preoperative frailty on postoperative outcomes after LVAD implantation is currently too limited to necessitate a practice change. Therefore, in line with the Iowa Model, this research project was designed and executed to further investigate the effect of preoperative frailty on postoperative outcomes in LVAD recipients. The results of this research will be added to the current body of evidence concerning this triggering issue and may be used to assess the need for practice change.

Review and Synthesis of the Evidence in the Literature

Search Methods

In line with the Iowa Model (Titler, 2001), a literature review was conducted to evaluate current evidence on the effect of preoperative frailty on postoperative outcomes after LVAD implantation. For this literature search, the electronic databases CINAHL, PubMed, and Academic Search Complete were searched for studies that evaluated the relationship between preoperative frailty and patient outcomes after LVAD implantation. The key word search terms used were *frailty* AND *left ventricular assist device* OR *heart assist device*. Criteria for inclusion were that the article be in English, from the year 2010 or later, and study adults. Articles were excluded if they were not original research studies, did not evaluate patients who underwent LVAD implantation, or did not quantify preoperative frailty using a tool and then relate this measure to post-implantation outcomes. This search strategy yielded 66 references that met inclusion criteria. Of these, 56 were excluded due to duplication or pre-determined exclusion criteria, leaving 10 articles for inclusion.

Synthesis of Evidence

Of the 10 studies included, three were retrospective chart reviews (Cooper et al., 2017; Herberton et al., 2016; & Jha et al., 2017); the remaining seven were prospective observational studies. The majority (6/10) used a Fried score of 3/5 or greater to determine frailty (Jha, et al., 2017; Joseph et al., 2017; Manghelli, et al., 2014; Reeves et al., 2016; Stein et al., 2019; & Uzun et al., 2019). Frailty was determined by handgrip strength in two studies (Chung et al., 2014 & Stein et al.,

2019) and by the following measures in one study: frailty deficit index (Dunlay et al., 2014), low psoas muscle mass (Herberton et al., 2016), and gait speed <0.8m/sec or by provider survey (Cooper et al., 2017). Outcomes assessed in these studies included mortality, length of stay, readmission rates, time mechanically ventilated, and several outcomes unique to individual studies. A syntheses table summarizing this literature review is included in Table 1.

Of the six studies which assessed long-term mortality, five found preoperative frailty to be associated with statistically higher mortality at 6 months and 1 year. Four of these studies (Chung et al. 2014; Cooper et al., 2017; Dunlay et al., 2014; Stein et al., 2019) reached statistical significance, while one did not (Jha et al., 2017). The last study found no difference between frail and non-frail patients (Joseph et al., 2017). The influence of frailty on short-term mortality in the postoperative inpatient period was assessed in 5 studies, all of which found that frailty was associated with increased inpatient mortality; however, none of these results reached statistical significance (Cooper et al., 2017; Herberton et al., 2016; Joseph et al., 2017; Manghelli et al., 2014; & Uzun et al., 2019).

Nine studies assessed the effect of frailty on postoperative length of stay (LOS), the majority of which (7/9) found that patients who were frail preoperatively had longer LOS. The results of 3 of these studies (Jha et al., 2017; Josesph et al., 2017; & Stein et al., 2019) reached statistical significance; however, 4 studies did not (Herberton et al., 2016; Manghelli et al., 2014; Reeves et al., 2016; & Uzun et al., 2019). Two studies, on the other hand, found that postoperative LOS did not differ significantly between frail and non-frail patients (Cooper et al., 2017 & Dunlay et. al, 2014).

Time mechanically ventilated postoperatively was also compared in three studies, all of which found that found that patients who were frail spent 24-68 hours longer on the ventilator than non-frail patients after LVAD implantation Two of these studies reached statistical significance (Joseph et al., 2017 & Mangelli et al., 2014), while the third did not (Jha et al., 2017).

Two studies assessed rehospitalization rates post- LVAD implantation and found readmission rates to be similar between frail and non-frail patients (Cooper et al., 2017 & Dunlay et al., 2014). Preoperative frailty was associated with significantly worse post-operative depression and quality of life (QOL) scores (Reeves et al., 2016), and increased (although not statistically significant) likelihood of discharge to rehab facility rather than home (Dunlay et. al., 2016).

Summary of Literature Review Findings and Gap in Evidence

Overall, the results of these studies demonstrate a clinically significant trend toward worse outcomes post-LVAD implantation for patients who were frail preoperatively, including increased inpatient and long-term mortality, length of stay, and time on ventilator; however, while some studies report significant results, many findings were not statistically significant, and two studies found no difference in long-term mortality and LOS (See Table 1). Frail patients did have significantly worse post-operative QOL and depression scores; however, these variables were assessed in only one study. Readmission rates were found to be similar between frail and non-frail patients in both studies assessing this outcome. Despite some variance in findings, it should be noted that no study reported better outcomes—and most demonstrate worse outcomes—for patients who are frail preoperatively than their non-frail counterparts.

Overall, relatively few studies—ten—evaluated the association between preoperative frailty and outcomes after LVAD implantation. Most studies (6/10) used Fried scores to determine frailty. All other metrics were utilized in two studies or less. No studies in this review employed use of the short SPPB to determine frailty and only one study used gait speed although these tools have been used reliably to assess frailty in patients advanced heart failure (Llopis et al., 2019 & Pandey et al., 2019). Outcomes such as ventilator time and readmission rates were evaluated in three or fewer studies, and postoperative QOL, depression, and discharge disposition were only assessed in one study each. And, while most studies assessed the influence of frailty on postoperative mortality and LOS, many of these studies failed to reach statistical significance (Cooper et al., 2016, Herberton et al., 2016, Jha et al., 2017, Joseph et al., 2017, Mangelli et al., 2014, Uzam et al, 2019).

While studies were of a moderate level of evidence (all were observational, non-experimental prospective or retrospective research studies), the overall strength of the evidence is relatively weak, as most studies had small sample sizes and many findings were not statistically significant. All but one of the studies (Cooper et al., 2017) were single center studies with small sample sizes of 44-100 patients; therefore, their results may be underpowered and lack generalizability. Unfortunately, the one study which was a multi-center study with a large sample size (Cooper et al., 2017) utilized a relatively subjective provider assessment of frailty and reported that there were gaps in the database from which information was gathered, which may put the study at risk for inaccuracies or bias.

There is a need for additional research concerning the effect of preoperative frailty on postoperative outcomes LVAD implantation. Additional research is needed to evaluate each of the outcomes discussed above in this review, especially quality of life, discharge disposition, and ICU LOS which were addressed by only one or two studies. Research evaluating preoperative frailty using measures which have not yet been studied with LVAD implantation—specifically SPPB, which is the tool we use at UK Hospital, or minimally studied (such as gait speed; i.e. the 6-MWT) is also needed. These are the gaps in current research this project aimed to address.

Methods

Design

This project was a descriptive research study with retrospective and prospective chart review designed to assess the relationship between preoperative frailty and postoperative outcomes after LVAD implantation. This study included advanced heart failure patients who had an LVAD implanted at UK Chandler Hospital between May 1, 2015 and April 30, 2020. Records from January 2015 to December 31, 2020 were accessed for this review.

Postoperative outcomes—hospital and ICU length of stay, postoperative time on ventilator, tracheostomy placement, discharge disposition, inpatient and 1-year mortality, readmission at 30 and 90 days after discharge, and change in pre- and post-operative quality of life scores—were compared between patients who were designated as frail or non-frail based on their previously documented 6-MWT or SPPB score. Demographic data and preoperative health data were collected and compared between the groups to determine if there is any significant difference between frail and non-frail groups and to assess whether any of these variables has a more significant influence on postoperative outcomes than preoperative frailty.

Setting

Agency Description. This project was conducted at the UK Chandler Hospital in Lexington, Kentucky. UK Chandler Hospital is a large, 945-bed, academic medical center that includes the Gill Heart Institute, a multidisciplinary team providing healthcare to patients with a wide range of cardiovascular conditions, including those with advanced heart failure who have undergone LVAD placement. Inpatient and outpatient care of LVAD patients is managed by the institution's Advanced Heart Failure team and a team of specially trained LVAD coordinators who coordinate pre-implant workup, post-operative care, and long-term health management of patients with a LVAD.

Project Congruence with Organizational Mission and Goals. As a key decision point in following the Iowa Model (Titler, 2001), concern for adverse outcomes after LVAD implantation as a result of preoperative frailty was determined to be a priority at UK Healthcare. UK Healthcare's mission statement emphasizes the organization's dedication to providing the most advanced care to the people of Kentucky and its commitment to the pillars of academic healthcare: research, education, and clinical care (UK HealthCare, n.d.). The organization is publicly committed to the value of innovation, stating that they "embrace continual learning and improvement to drive positive change" (UK HealthCare, n.d.). It is a goal of the Gill Heart Institute to excel in clinical outcomes in cardiovascular health and disease by using quality outcomes and research data to drive continuous improvements (UK HealthCare, 2015). In pursuit of this goal, the team of heart failure providers and cardiovascular surgeons at UK Healthcare closely track and work to improve postoperative outcomes after LVAD placement.

The aim of this project was to understand more about whether preoperative frailty negatively influences postoperative outcomes after LVAD implantation and whether the SPPB and 6-MWT can add significant prognostic information to aid in the selection of patients for LVAD implantation to prevent harm and improve patient outcomes. This objective aligns with the goals and mission of UK Healthcare and addresses the issue of potentially worse outcomes after LVAD implant because of frailty, which is a priority at the institution.

Stakeholder Identification. Stakeholders influential to my project include the mechanical circulatory support (MCS) team who coordinate care for LVAD patients, the physical therapists who evaluate and work with patients before and after LVAD implantation, the heart failure providers who care for LVAD patients, cardiothoracic surgeons who implant LVADs, and the patients with heart failure who receive LVADs. The hospital's MCS LVAD coordinators helped to provide information concerning data collection pre- and post-LVAD implantation for this project. Several physical therapists who evaluate patients pre- and post-implantation also took interest in this project and provided detailed information concerning the process of frailty assessment at UK Hospital using 6-MWT and SPPB score. At the completion of this project, results will be shared with these stakeholders to address their potential influence on current practice.

Patients who undergo LVAD implantation at UK Hospital are this study's target population, and are, thus, also important stakeholders. Ultimately, the results of this project may influence the selection and education of future patients concerning the risks and benefits of LVAD implantation associated with their level of frailty.

Site-Specific Facilitators and Barriers to Implementation. There are several site-specific factors which helped to facilitate implementation of my project. As described above, this project aligned with UK Healthcare's mission and goals of conducting outcomes research in order to promote best practice and improved patient outcomes. Additionally, the MCS manager and coordinators and physical therapists were willing to offer expertise and help facilitate data collection.

As the design of this project was a chart review, it did not require a large amount of space, personnel, or financial resources to implement.

In addition to these facilitators, there were also several factors which served as barriers to data collection. 6-MWT and SPPB scores are documented in inconsistent locations within the EMR and were not documented on every patient postoperatively. There is also no efficient, accurate way to assess time mechanically ventilated or LOS after LVAD implantation surgery; therefore, each of these outcomes had to be manually audited. Pre- and postoperative QOL scores were documented on paper charts, and, although every patient is supposed to have these assessments documented pre-implantation and at 6 months and 1 year after discharge, the majority were missing this documentation. Post-operative 6-MWT were also documented at inconsistent points in time postoperatively. These barriers made data retrieval more time consuming and resulted in missing data for some outcomes.

Sample

The sample for my study included 120 adult patients with advanced heart failure who had a LVAD implanted at UK Chandler Hospital between May 1, 2015 and April 30, 2020. This sample includes adult patients of varying age, gender, race, socio-economic and education backgrounds from the state of Kentucky as well as multiple surrounding states.

Patients were identified for inclusion to this study through chart review. Criteria for inclusion were that patients: 1) had undergone LVAD implantation at University of Kentucky Hospital between May 1, 2015 and April 30, 2020, and 2) had documentation of preoperative 6-MWT and/or SPPB score *or* documentation indicating inability to complete these assessments due to frailty or medical condition. Patients were excluded if they had no documentation discussing preoperative frailty assessments. Of the 129 patients who were identified for inclusion, 9 were excluded based on predetermined criteria, leaving 120 patients to be included in the final sample.

Procedure

IRB Approval. Prior to initiation of data collection, approval was obtained from the University of Kentucky Institutional Review Board to conduct this project through exemption certification.

Measures and instruments. Preoperative frailty was determined using documented preoperative 6-MWT and SPPB scores. The assessments documented most recently before LVAD implantation, and no more than 6 months prior to implantation, were utilized in this study.

A 6-MWT is measured by timing the distance a patient walks in 6 minutes in an unobstructed hallway or around a track. The 6-MWT is a widely used measure to assess physical performance in patients with heart failure (Yamamoto et. al, 2020) and has been used reliably to determine frailty in patients with heart failure (intra-class co-efficient of 0.9; $p<0.0001$) (Uszko-Lenscer, 2017). Established guidelines for conducting 6-MWTs have been released by the American Thoracic Society to help providers reliably reproduce the assessment (Holland et al., 2014). 6-MWT has also been determined to be valid tool to assess frailty in patients with heart failure. Progressive decline in distance walked during the 6-MWT is associated with progressive decline in peak aerobic capacity and progressive decline in other measures of physical performance like Fried scores and shuttle walks (Boxer et al., 2010, Giannitsi, 2019). Shorter distances walked are also associated with worse clinical outcomes such as increased mortality for patients with heart failure (Giannitsi, 2019; Yamamoto et. al, 2020).

Different distance cutoffs, usually ranging from 200-300 meters have been used to determine frailty in patients with heart failure. Yamada and colleagues (2015), as well as Guazzi and colleagues (2009), found a 6-MWT of <300 meters to be associated with a significantly higher risk of mortality in patients with heart failure, while a cutoff of <200 meters or less predicted increased mortality in other studies (Alahdab, 2009; Curtis et al., 2004). In a study conducted by Yap and colleagues

(2015), the inability to walk a distance of 225 meters or more was found to be predictive of worse clinical outcomes for patients in NYHF classes III and IV.

When evaluating my sample, 80.8% of patients walked less than 300 meters and 53.3% walked less than 200 meters during their preoperative 6-MWT. In other research studies assessing the effect of frailty on postoperative outcomes after LVAD implantation, frailty prevalence ranged from 22.2 % to 75% (Chung et al., 2014; Reeves et al., 2016). A 6-MWT of <200 meters was, therefore, used to define frailty in this study, as the sample's prevalence of frailty using this cutoff better correlated with the prevalence of frailty in other studies, and 200 meters has been previously used to define frailty in patients with advanced heart failure. As many patients undergoing LVAD implant are typically in NYHF classes III-IV, a 6-MWT less than 200 meters may more closely predict negative outcomes in this population as well.

The SPPB test consists of 3 components: standing balance, gait speed, and timed repeated chair rises. Each of the components is scored on a scale of 0 to 4 and combined for a total score ranging for 0 to 12, with a lower score indicating greater functional impairment. A copy of the SPPB assessment is provided in Appendix B. The SPPB score is a well-established tool that provides reproducible measurement of physical function in older adults and has been used to determine frailty in patients with heart failure (Pandey et al., 2019; Chiarantini et. al, 2010). A score of less than 8 has been found to best predict frailty with sensitivity (79.9%) and specificity (73.8%) (Perracini et. al, 2020) and to be associated with low grip strength (OR 2.45, $p<0.05$) and falls (OR 1.49, $p<0.05$)((Ramírez-Vélez, 2020). In this study, therefore, patients were, considered frail if they had a score less than or equal to 7 of 12.

The postoperative outcomes assessed in this study were inpatient and one-year mortality, hospital LOS and ICU LOS, time mechanically ventilated, tracheostomy placement, discharge disposition, hospital readmissions at 30 and 90 days, and change in pre- and post-operative QOL scores. Inpatient mortality and 1-year mortality were determined by presence of a documented date of death during initial postoperative hospitalization or within the first year after LVAD implantation. Post-operative tracheostomy placement was determined by presence of documented tracheostomy operative note. For patients who survived to discharge, LOS and ICU LOS were measured in days. Postoperative time on mechanical ventilation was measured in cumulative hours of documented time mechanically ventilated. Hospital readmissions at 30 and 90 days were determined by presence of admission H&P documented within 30 or 90 days after postoperative hospitalization discharge date.

Change in pre- and postoperative quality of life scores were measured using the difference between pre- and postoperative 3-level EuroQol 5 Dimensions Questionnaire (EQ-5D-3L) scores and 12-item Kansas City Cardiomyopathy questionnaire (KCCQ-12) scores. The EQ-5D-3L is a self-completed patient questionnaire assessing 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression and has been found to assess quality of life reliably for patient with cardiac conditions and after cardiac surgery (Schweikert, Hahmann, & Leidl, 2006; Heiskanen et al., 2016). Maximum score is 25 points, with higher scores indicating higher reported QOL. The KCCQ-12 is a 12-item self-completed patient questionnaire and is a validated tool for assessing quality of life in patients with heart failure (Spertus & Jones, 2015). Maximum score is 64 points, with higher scores indicating higher reported QOL.

Other demographic and baseline health data, including age, gender, race, heart failure classification, and comorbidities as well as postoperative 6-MWT (which was measured as described above and documented within the first postoperative year), were collected to compare frail and non-frail groups and to assess confounding variables. A table listing study variables and their measures is included in Appendix C.

Data Collection. Study personnel obtained a list of medical record numbers for patients who had undergone LVAD implantation at UK Chandler Hospital between May 1, 2015 and April 30, 2020 from UK Healthcare's LVAD coordinating team. This list was used to conduct a chart review of retrospective and prospective data from patients' electronic and paper medical records.

Records from January 2015 to December 31, 2020 were accessed for this review. Data prospectively collected included inpatient and one-year morality and postoperative EQ-5d-3L and KCCQ-12 quality of life assessments documented as part of routine care provided within the data collection period which lasted from September 1, 2020 to January 31, 2021. All other data was retrospectively collected.

Data Analysis. Data analysis was conducted using IBM SPSS Statistics Version 26 software with the guidance of a university statistician. Demographic and baseline health data, and frailty prevalence were analyzed using descriptive statistics. Bivariate statistics including Chi-Square and Fischer's exact tests, independent samples t tests, and Mann-Whitney tests were used to assess the association between each measure of frailty and postoperative outcomes and to compare demographic and health characteristic data between frail and non-frail groups. McNemar test was used to compare patients' preoperative 6-MWT with their post-implant performance.

Logistic regression models were used to examine predictors of tracheotomy placement, discharge disposition, one-year mortality, hospital and ICU LOS, and time mechanically ventilated. Because the distributions for hospital LOS, vent hours and ICU LOS were right skewed, we created binary (yes/no) variables for whether the patient experienced the outcome greater than the 75th percentile. Cutoffs were LOS greater than 33 days, ICU LOS greater than 18 days, and greater than 101 hours mechanically ventilated. Each logistic regression model included the two measures of frailty along with age, gender, BMI, previous sternotomy, preoperative reduction in RVEF, and comorbid conditions (DM, COPD, HTN, PHTN).

Level of significance was set at $P \leq 0.05$ for all analyses.

Results

Frailty prevalence

120 of the 120 patients included had documented preoperative 6-MWTs. Overall mean 6MWT was 191.71 (± 110.7) meters. 53.3% of patients (n=64) had 6-MWT of 200 meters or less, which identified them as frail for purposes of this study.

112 of the 120 patients had documented SPPB tests. Overall mean SPPB score was 7.55 (± 4.06). 41.1% of patients (n=46) had a SPPB score of 7/12 or less and were identified as frail for purposes of this study.

Demographics and baseline health data

Overall mean age was 53.9 years (range 18-83). 84.2% of the overall sample were male; 90.0% were Caucasian. Mean cardiac index was 1.83 L/min/m^2. 84% of patients had an EF less than 20%, 20.8% had had a previous sternotomy, and 54.2% had moderate or severely reduced RVEF. Overall sample demographic and preoperative health variables, as well as the breakdown between frail vs non-frail patient characteristics based on cutoff scores of 6-MTW <200m and SPPB ≤ 7/12, are in included in Table 2.

When 6-MWT < 200m was used to determine frailty, the only significant difference between frail and non-frail groups was the percentage of those with diabetes (DM). A significantly larger percent of frail patients had DM (62.5%) than non-frail patients (41.1%) (p=0.019). When SPPB ≤ 7/12 was used to determine frailty, the only significant difference between the frail and non-frail groups was in NYHF classification/AHA stage. 91.3% percent of frail patients were class IVd, with the remaining 8.7% in classes IIIc and IIId, while 75.8% of non-frail patients were classified as IVd and 24.3% were in class IIIc or IIId (p=0.035).

Outcomes and 6-MWT <200m

Frailty defined by 6-MWT < 200 meters was associated with a statistically significant increase in 1-year mortality, with 31.3% mortality at one year for frail patients and 13.2% for non-frail patients (p=0.021). Inpatient mortality was not significantly different between frail and non-frail groups (10.9% vs 8.9%, p=0.714).

Frailty defined by 6-MWT < 200 meters was associated with a statistically significant increase in hospital LOS with a median LOS of 24 days (IQR 17.25-43 days) for frail patients and 19 days (IQR 15-26 days) for non-frail patients (p=0.021). Frail patients were found to have a median ICU LOS of 13 days (IQR 8-21.75) while non-frail patients were found to have ICU LOS of 10 days (IQR 7-13), although this difference did not reach statistical significance (p=0.059).

6-MWT < 200 meters was associated with increased time mechanically ventilated. Patients with 6-MWT < 200 meters were mechanically ventilated for a median of 71.25 hours (IQR 22.63-136.25h), while non-frail patients were mechanically ventilated for a median of 22.0 hours (IQR 17-50.5h) (p <0.001). Frailty as defined by 6 MWT <200 meters was also associated with increased tracheostomy placement, with 23.8% of frail patients requiring tracheostomy placement compared to 5.5% of non-frail patients (p=0.006).

6-MWT < 200 meters was also associated with increased discharges to inpatient rehab facilities/long term care facilities as opposed to home. 47.4% of patients with preoperative 6-MWT < 200 meters were discharge to an inpatient facility, while only 11.8% of non-frail patients were (p<0.001).

30- and 90-day readmissions were not statistically significant between frail and non-frail groups, when 6-MWT < 200 meters determined frailty. 25% of frail patients were readmitted within 30 days and 17.6% of non-frail patients were readmitted with 30 days of discharge after implantation (p= 0.355). 41.1% of frail patients, versus 41.2% of non-frail patients, were readmitted within 90 days of discharge after implant (p=0.991).

Only 12 patients had both pre and post KCCQ-12 assessments documented, and only 19 had both pre- and post-EQ-5D-3L assessments documented. Of those with EQ-5D-3L scores documented, 8 were considered frail and 11 were not. Of those with KCCQ-12 documented, 6 were frail based on 6MTW <200 m, and 6 were non-frail. There was no significant change in preoperative and postoperative QOL scores between frail and non-frail groups. For the EQ-5D-3L assessment, mean increase in score was 4.88 pts for frail patients and 3.82 points for non-frail patients ($p=0.439$). For the KCCQ-12 assessment, mean increase in score was 17.67 point for frail patients and 11.6 points for non-frail patients ($p= 0.206$).

Outcomes and SPPB score ≤ 7/12

Frailty as defined by SPPB score of 7/12 or less was associated with a statistically significant increase in 1-year mortality, with 33.3% mortality at one year for frail patients and 15.6% for non-frail patients ($p=0.030$). Inpatient mortality was not significantly different between frail and non-frail groups (13.0% vs 9.1%, $p=0.546$).

Frailty as defined by SPPB score ≤ 7/12 was associated with a statistically significant increase in hospital LOS, with a median LOS of 31 days (IQR 21-45 days) for frail patients and 18.5 days (IQR 15-26 days) for non-frail patients ($p<0.001$). With this measure, frailty was also associated with a statistically significant increase in ICU LOS. Median ICU LOS was 15 days (IQR 11-34 days) for frail patients and 9.5 days (IQR 7-13.75 days) for non-frail patients ($p<0.001$).

SPPB score ≤ 7/12 was associated with increased time mechanically ventilated. Frail patients with SPPB score ≤ 7/12 were mechanically ventilated for a median of 81 hours (IQR 23-308h), while non-frail patients were mechanically ventilated for a median of 22.75 hours (IQR 18.5-60.63h) ($p <0.001$). SPPB score ≤ 7/12 was also associated with increased tracheostomy placement, with 31.1% of frail patients requiring tracheostomy placement compared to 4.6% of non-frail patients ($p<0.001$).

SPPB score of 7/12 or less was associated with increased discharges to inpatient rehab facilities/long term care facilities as opposed to home. 55.0% of patients with SPPB score ≤ 7/12 were discharged to an inpatient facility, while 16.7% of non-frail patients were ($p<0.001$).

30- and 90-day readmissions were not statistically significant between frail and non-frail groups, when SPPB score ≤ 7/12 was the cutoff for frailty. 20% of frail patients were readmitted within 30 days and 18.6% of non-frail patients were readmitted with 30 days of discharge after implantation ($p= 0.886$). 40.0% of frail patients versus 37.3% of non-frail patients were readmitted within 90 days of discharge after implantation ($p=0.785$).

There was also no significant change in preoperative and postoperative QOL scores between frail and non-frail groups, although there was a significant amount of data missing for this outcome. Of patients with documented SPPB scores, only 7 patients had both pre and post KCCQ-12 assessments documented, and only 13 had both pre- and post-EQ-5D-3L assessments documented. Of those with EQ-5D-3L scores documented, 6 were considered frail and 7 were not. Of those with KCCQ-12 documented, 5 were frail based on SPPB score, and 2 were not frail. For the EQ-5D-3L assessment, mean increase in score was 4.80 pts for frail patients versus 4.1 points for non-frail patients ($p=0.715$). For the KCCQ-12 assessment, mean increase in score was 15.8 point for frail patients and 11.0 points for non-frail patients ($p= 0.371$).

Outcomes results for frail and non-frail groups according to each frailty measure cutoff are summarized in Table 3.

Comparison of pre- and post-operative 6-MWT

Ability to walk ≥ 200 meters during preoperative 6-MWT was not significantly associated with the same ability after LVAD implantation ($p=0.572$). Of the 42 patients who could walk 200 meters or more preoperatively, 26 (61.9%) could do so postoperatively, while 16 (38.1%) could not. Of the 40 patients who walked less than 200 meters preoperatively, 28 (70.0%) still did not walk over 200 meters after LVAD implantation, while 12 (30.0%) now could.

Logistic Regression Models

In modeling tracheotomy, SPPB score ≤ 7 was the only significant variable in the model; those with frailty defined by SPPB score ≤ 7 were 9 times more likely to have a trach compared to those with non-frailty ($OR = 9.4$, $p=.01$). In modeling predictors of hours mechanically ventilated, SPPB score ≤ 7 was also the only significant variable; those with frailty defined by SPPB score ≤ 7 were 7.5 times more likely to be in the upper quartile (>101 hours) of those mechanically vented (OR 7.5; P= 0.04).

In modeling discharge to another facility rather than home, SPPB ≤ 7 (OR = 7.5, p=.006), older age (OR= 1.1, p=.002) and female sex (OR = 7.8, p =.019) were significant predictors. For logistic regressions modeling hospital and ICU LOS, both SPPB score ≤ 7 (hospital: OR 6.5, p= 0.007; ICU: OR 4.7; p=0.023) and age (hospital: OR 1.1, p=0.021; ICU: OR 1.1, p=0.029) were predictors in these models. After adjusting for age, gender, BMI, and comorbid conditions, no variable was a significant predictor of 1-year mortality, including SPPB score.

In no model was 6-MWT found to be a statistically significant predictor of the outcome evaluated after adjustment for age, gender, BMI, previous sternotomy, preoperative reduction in RVEF, and other comorbidities,.

Discussion

For this study, preoperative frailty was independently determined using both 6-MWT of 200 meters or less and SPPB score of 7/12 or less. In the same sample, more patients were considered frail using 6-MWT < 200 meters than SPPB score ≤ 7/12, which may indicate that SPPB ≤ 7/12 provides a stricter cutoff point. The prevalence of frailty as determined by either of this study's measures falls within the range found in other studies of patients undergoing LVAD implantation. Frailty prevalence was as low as 22.2% when hand grip strength was used to determine frailty (Chung et al., 2014) and ranged from 47.5 to 75% in studies using Fried score of ≤ 3/5 to determine frailty (Jha et al., 2017; Reeves et al., 2016).

Overall, frailty was associated with worse postoperative outcomes for patients who were identified as being frail preoperatively. Based on the determination of frailty as 6-MWT < 200 meters, patients who were identified as frail had a significant increase in 1-year mortality, hospital LOS, hours mechanically ventilated, tracheostomy placement, and discharge to inpatient facility rather than home. Those who were identified as frail using SPPB score of 7/12 or less also had a significant increase in these negative outcomes, as well as longer ICU LOS. There was no significant difference in inpatient mortality, 30- or 90-day readmission rate, or change in pre-/post-operative QOL scores between frail and non-frail groups for both frailty measures.

Frailty was associated with increased 1-year mortality for both measures of frailty and was similar between the two measures. 1-year mortality for frail and non-frail groups was 31.3% vs 13.2% when frailty was defined as 6 MTW <200 meters (p=0.021) and 33.3% vs 15.6% when frailty was defined as SPPB score ≤ 7/12 (p=0.030). When either measure was used to determine frailty, 1-year mortality was more than doubled for frail patients. This finding further confirms the results of other studies which used different measures (such as Fried score) to compare frailty and post-implant mortality, as the majority (4/6) found preoperative frailty to be associated with a statistically significant increase in mortality at 6 months or 1 year (Chung et al. 2014; Cooper et al., 2017; Dunlay et al., 2014; Stein et al., 2019). Although frailty was associated with increased 1-year mortality, inpatient mortality was not significantly different between frail and non-frail groups in this study, regardless of the measure used to determine frailty. This finding is similar to those of previous studies, as none found a statistically significant difference in inpatient mortality between frail and non-frail patients after LVAD implantation (Cooper et al., 2017; Herberton et al., 2016; Joseph et al., 2017; Manghelli et al., 2014; & Uzun et al., 2019).

Frailty was also associated with a statistically significant increase in LOS when defined by either measurement. When a cutoff of 6-MWT <200 meters was used, median hospital LOS was 24 days for frail patients and 19 days for non-frail patients (p=0.021). An even larger difference was noted when a when cutoff of SPPB ≤ 7/12 was used: median hospital LOS was 31 days for frail patients and 18.5 days for non-frail patients (p<0.001). Currently, 7/9 studies have found that patients who were frail preoperatively had longer postoperative LOS as discussed in the literature review; however, only three of these reached statistical significance (Jha et al., 2017; Joseph et al., 2017; &

Stein et al., 2019). The results of this study, therefore, provide further confirmation that preoperative frailty is indeed associated with increased hospital LOS.

Frailty as defined by SPPB ≤ 7/12 was also associated with a statistically significant increase in ICU LOS, with a median ICU LOS of 15 days for frail patients and 9.5 days for non-frail patients ($p<0.001$). Patients determined to be frail by 6-MWT <200m also had a trend to toward increased ICU LOS: median ICU LOS for frail patients was 13 days and 10 days for non-frail patients using this measure, although this difference did not reach statistical significance ($p=0.059$). These finding agree with those the only current study assessing ICU LOS (Jha et al., 2017) who found that ICU LOS was significantly longer (12 vs 6 days) for frail patients.

Patients who were designated as frail by either measure also had a statistically significant increase in time mechanically ventilated. Those with 6-MWT <200m were mechanically ventilated for a median of 71.25 hours, compared to a median of 22.0 hours for non-frail patients ($p <0.001$). Those with SPPB score ≤ 7/12 were mechanically ventilated for a median of 81 hours, while non-frail patients were mechanically ventilated for a median of 22.75 hours ($p <0.001$). This is notable, as the median time mechanically ventilated for non-frail patients by either measure was less than one day, whereas those who were frail spent closer to 3 days mechanically ventilated after LVAD implantation and were much more likely to need prolonged mechanical ventilation. This difference is especially pronounced when SPPB ≤ 7/12 was used to determine frailty, as 25% of frail patients according to this measure were mechanically ventilated over 308 hours, which is longer than 12 days.

Time mechanically ventilated postoperatively has been compared in three previous studies, all of which found that found that patients who were frail spent a median of 24-68 hours longer on the ventilator than non-frail patients after LVAD implantation. Two of these studies reached statistical significance (Joseph et al., 2017 & Mangelli et al., 2014), while the third did not (Jha et al., 2017). As these studies had relatively small sample sizes (n=40-75), the result of this study help to affirm their findings and increase the power of results. As increased time mechanically ventilated is associated with increased risk for complications like delirium, muscle weakness, pressure injuries, ventilator associated pneumonia, sepsis, and increased mortality after cardiac surgery (Loss et al., 2015; Papathanasiou et al., 2019), its association with frailty is certainly important.

Tracheostomy placement was also significantly higher in patients who were determined to be frail preoperatively by either measure, although the difference was greater when SPPB was used to determine frailty. When frailty was defined as 6-MTW <200 meters, 23.8% of frail patients required tracheostomy placement, compared to 5.5% of non-frail patients (p=0.006). When frailty was defined as SPPB score of 7/12 or less, 31.1% of frail patients required tracheostomy placement compared to 4.6% of non-frail patients (p<0.001). This difference is certainly notable as approximately 1 in 20 non-frail patients required a trach, whereas almost 1 in 3 frail patients did.

This study was the first to assess the association between preoperative frailty and postoperative tracheostomy placement after LVAD implantation, and both clinically and statistically significant results were found. While tracheostomy placement facilitates ventilator weaning, reduces the need for heavy sedation, and allows for enhanced mobility for those requiring prolonged mechanical ventilation (Devarajan et al., 2012; Troullitt et al., 2009), its placement has also been associated with patient discomfort, untoward effects on speech and swallowing abilities, and decreased long term quality of life and body image perception (Bach 1993; Gilony 2005; Vargas et al., 2018). As frail patient have much higher likelihood of requiring tracheostomy postoperatively, this is an important potential outcome to discuss with patient as they undergo consideration for LVAD implantation.

Frailty, when defined by either of this study's measures, was also associated with a statistically significant increase in discharges to acute rehab/long term care facilities, as opposed to home. When 6-MWT <200 meters determined frailty, 47.4% of frail patients were discharged to an inpatient facility compared to 11.8% of non-frail patients (p<0.001). When SPPB score ≤ 7/12 was used to determine frailty, 55.0% of patients deemed frail were discharged to an inpatient facility, compared to 16.7% of non-frail patients ($p<0.001$). Currently only one other study (Dunlay et. al., 2016), which found a non-statistically significant increase in the likelihood of discharge to rehab facility rather than home, had evaluated this outcome. This study further supports the association between preoperative frailty and increased likelihood of discharge to an inpatient facility rather than home after LVAD implantation.

It may seem intuitive that frail patients will need more rehabilitation services postoperatively than their non-frail counterparts, which has been the case after other types of cardiac surgery (Bergquist et al., 2018). Current research, however, was unclear as to whether frail patients would have the same needs after a LVAD implantation, as this device is designed to improve heart failure symptoms and could potentially reverse frailty. This study demonstrates that patients who are frail preoperatively will likely require more intense rehab services postoperatively and are less likely to be discharged home than those who are not frail. Although this is not necessarily a bad thing, it is important to inform patients of the potential need for inpatient rehab services in order to shape their understanding of the recovery process after LVAD implantation. Such insight may also help to facilitate earlier discharge planning.

In this study, 30- and 90-day readmissions were not significantly different between frail and non-frail groups in this study, regardless of which measure was used to determine frailty. This finding is similar to the other two studies which have assessed rehospitalization rates post- LVAD implantation, both of which found readmission rates to be similar between frail and non-frail patients (Cooper et al., 2017 & Dunlay et al., 2014). Reasons for readmission were also similar between groups with GI bleed, HF exacerbation symptoms, altered mental status, and LVAD alarms and complications being the most prevalent.

There was also no significant change in preoperative and postoperative QOL scores between frail and non-frail groups, regardless of the measure used to determine frailty; although, there was a significant amount of data missing for this outcome which may have influenced the fidelity and/or power of results. Interestingly, although not a statistically significant finding, mean increase in QOL scores was higher for patients who were frail preoperatively. This may indicate that receipt of an LVAD stands to improve QOL more for patient who are frail. Although other outcomes may be worse for patients who are frail pre-implant compared to their non-frail counterparts, they still may experience better quality of life after implantation than they did before.

Only one other previous study has assessed the influence of frailty on QOL after LVAD implantation. Reeves and colleagues (2016) found that patients who were frail preoperatively had significantly lower QOL scores than non-frail patients. They, however, assessed only postoperative surveys, whereas in this study, change in pre-and post-surveys were compared. As QOL is subjective, an individual's change in QOL over time may more accurately reflect the influence of frailty on this outcome after implantation. As this study was missing a considerable amount of data, further research is still certainly needed to investigate this topic.

While both measures of frailty demonstrated statistically significant differences between frail and non-frail patients in tracheostomy placement, discharge to inpatient facility rather than home, 1-year mortality, hospital LOS, and hours mechanically ventilated in bivariate statistical analyses, SPPB score $\leq$ 7/12 was the only frailty measure predictive of negative outcomes in logistic regression models. After adjustments were made for age, gender, BMI, previous sternotomy, preoperative reduction in RVEF, and other comorbid conditions, patients determined to be frail by SPPB score $\leq$ 7/12, were 9.4 times more likely to have a tracheostomy placed ($p=0.01$) and 7.5 times more likely mechanically ventilated for a prolonged period of time (>101 h) ($p= 0.04$). Patients with SPPB score $\leq$ 7/12 were 6.5 times more likely to have prolonged hospital LOS ($p= 0.007$), 4.7 times more likely to have prolonged ICU LOS ($p=0.023$) and were 7.5 times more likely to be discharged to an inpatient facility rather than home ($p=0.01$). 6-MWT <200m, on the other hand, was not found to be a significant predictor of any outcomes in the models, which points to the superiority of SPPB $\leq$

7/12 in predicting negative outcomes, even when adjustment are made for age, gender, BMI and comorbidities.

Interestingly, few variables other than SPPB score were significant predictors of negative outcomes. SPPB ≤ 7/12 was the only significant predictor of time mechanically ventilated and tracheostomy placement. There only one instance where another variable was a stronger predictor of an outcome than SPPB: female sex had a higher OR (7.8) than SPPB ≤ 7/12 (OR 7.5) for predicting discharge to inpatient facility. Older age was also a predictor of increased hospital LOS, ICU LOS, and discharge to an inpatient facility rather than home, although the odds ratio was 1.1 for each of these outcomes, which is much lower than those associated with SPPB score ≤ 7/12. Overall, the logistic regression models demonstrated that frailty defined by SPPB ≤ 7/12 consistently predicted negative outcomes better than any other baseline demographic or health variable

The original plan for this project included analysis of postoperative 6-MWT in the logistic regression models to assess whether postoperative frailty was a stronger predictor of outcomes (see objective 5). This analysis was ultimately foregone as the timing of documentation of postoperative 6-MWTs was quite variable, ranging from inpatient stay after implantation to anytime during the first postoperative year, and there was concerns that this would affect the fidelity the analysis of outcomes primarily experienced inpatient. Results of 6-MWT were still compared pre- and post-operatively.

In this analysis, ability to walk ≥200 meters on 6-MWT was not significantly associated with the same ability after LVAD implantation (p=0.572). Of the 42 patients who could walk 200 meters or more preop, 26 (61.9%) could do so postop, while 16 (38.1%) could not. Of the 40 patients who walked less than 200 meters preop, 28 (70.0%) still did not walk over 200 meters after LVAD implantation, while 12 (30.0%) now could. So, while 6-MWT improved for 30% of frail patients (suggesting that frailty may be reversible), it also worsened for 38.1% of non-frail patients. However, as 6-MWT were recorded at differing times within the first postoperative year, results may have been influenced by this variation. More prospective research is needed to look at scores at different time interval, during inpatient postop, at 6 months, and at 1 year, for example, to determine if/how scores change and then relate scores to postoperative outcomes.

Impact on site and next steps

This project had little impact on the site as it was being conducted due to its design as a mostly retrospective chart review. Findings from the data collection phase did reveal that there was a lack of consistency in documenting pre- and postoperative QOL assessments and in the timing of when postoperative 6-MWT are conducted. This may be due to several reasons including current lack of priority placed on QOL and postoperative 6-MWT assessment or lack of staff/time to complete these assessments. A next step in furthering this research project would be to continue this project prospectively, with research personnel helping to collect data for QOL assessments and post-operative 6-MWTs prospectively to ensure consistent collection and documentation of this data. The association between preoperative frailty and change in QOL after implantation could then be better analyzed. 6-MWTs consistently collected in the postoperative period before discharge as well as at one year could be used to assess change in frailty after surgery as well as determine whether postoperative frailty is a stronger predictor of negative outcomes than preoperative frailty.

The results of this project will be disseminated to stakeholders including the LVAD coordinating team, physical therapists, and cardiovascular surgeons who care for patients who undergo LVAD implantation at UK hospital as next step for this project.

Implications

In line with the Iowa Model (Titler, 2001), results of this research can be used to inform evidence-based practice change. LVADs are increasingly being implanted in patients with heart failure, especially those who are not candidates for transplant due to presence of concomitant comorbidities or age. These patients are often frail preoperatively. As frailty is associated with worse postoperative outcomes—specifically increased 1-year mortality, hospital and ICU LOS, hours mechanically ventilated, need for tracheostomy placement, and discharge to inpatient facility rather than home—frailty assessment should not only be completed on patients prior to LVAD implantation, but also incorporated into the LVAD candidate selection and education process. SPPB and 6-MWT are easily conducted assessments that require little equipment and minimal training from staff to complete. Results of these preoperative frailty assessments can be used by providers to weigh individuals' personal risks versus the benefit of LVAD implantation surgery when determining candidacy. While frailty is just one factor to consider, it may serve as an important high-risk marker to help identify patients who may least benefit from device placement or who may require more resources, closer follow-up, and more aggressive rehabilitation postoperatively. Results of frailty assessments can also be used to better inform patients of more personalized risks associated with this procedure based on their personal level of frailty and the likelihood of outcomes such as longer LOS, tracheostomy placement, and discharge to rehabilitation facility if they are identified as frail. This will help patients make informed decision concerning whether or not to undergo device implantation as well as shape their expectations concerning the postoperative recovery process.

While both 6-MWT <200m and SPPB ≤ 7/12 were both associated with significantly worse outcomes for frail patients, after correcting for age, gender, BMI, previous sternotomy, RVEF, and other comorbidities, SPPB was a significant, and much stronger predictor of negative outcomes than 6-MWT. Therefore, SPPB ≤ 7/12 is likely a better measure to use to determine frailty in this population.

As this was the first study to compare frailty as defined by SPPB ≤ 7/12 to 6-MWT < 200 meters when assessing outcomes after LVAD implant, it may be desirable to reproduce a similar study at other facilities to confirm the results found here. Future research comparing different measures of frailty, such as one comparing SPPB score with Fried score or handgrip strength, is also needed to determine which frailty measure is the best predictor of outcomes in patients undergoing LVAD implantation.

Additionally, there is a need for more prospective research concerning frailty and QOL after LVAD implantation. This study had a significant amount of missing QOL data and was unable reach statistical significance. In this study, patient who were frail preoperatively had larger, although not statistically significant, improvements in QOL scores. This topic is certainly worth further investigation, as frail patients may stand to experience better quality of life after implantation, despite experiencing worse postoperative outcomes than non-frail patients. For some patients, this may be considered the most important outcome.

Prospective studies comparing 6-MWT time or other measure of frailty (like SPPB or Fried score) preoperatively and at consistent intervals postoperatively would also be useful in helping to determine how frailty is modified over time after LVAD implantation and if change in frailty after implantation is a stronger predictor of inpatient and longer-term outcomes. As postoperative 6-MWTs were collected at varying points throughout the first postoperative year, such an analysis could not be conducted for this study.

Lastly, research investigating whether targeted interventions can improve frailty in patients with heart failure is also needed. Currently, one such study, the REHAB-HF study is in progress. The REHAB-HF is a NIH funded, randomized controlled trial assessing whether a 12-week rehabilitation intervention improves frailty in patients with acute decompensated heart failure (Kitzman, NCT02196038). If frailty can be improved using such interventions, efforts could be made to improve frailty prior to LVAD implantation in order reduce the risk of negative postoperative outcomes associated with frailty.

Limitations

This was a single center study of 120 patients. Although, this sample is fairly sizable for a single center study of patients who underwent LVAD implantation—a procedure performed with limited frequency and at a limited number of institutions—there is still the potential that sample size may have underpowered the results. As this was a single center study with a majority male, Caucasian sample with non-ischemic cardiomyopathy, one must be careful when generalizing these results to other populations or at other institutions.

Additionally, this is a descriptive study with the majority of data being retrospectively collected. As a result, temporal bias may have influenced this study. As data was collected through retrospective chart review of documentation completed by other healthcare providers, the completeness/accuracy of documentation could not be controlled by study personnel. As discussed previously, postoperative 6-MWTs were documented at inconsistent intervals postoperatively, which may have influenced the validity of the comparison between patients pre- and postoperative results. Additionally, due to this inconsistency, postoperative 6-MWT could not be assessed as a stronger predictor of negative outcomes than preoperative frailty in our logistic regression models.

A large amount of data was also missing for pre- and postoperative QOL assessments. In total, only 12 patients had both pre and post KCCQ-12 assessments documented, and only 19 had both pre- and post-EQ-5D-3L assessments documented. With such a small number of completed assessments, results concerning frailty and QOL scores were underpowered and potentially biased, which limits the utility of these particular results. It may also be important to note that results of QOL scores can only be collected from patients who survive, return to clinic, and are able to complete the papers surveys by themselves or with the assistance of a member of the healthcare team. This may inflate post-survey scores as those who experienced more morbidity after LVAD implantation may not be able to complete 6 month-1year follow up surveys.

Lastly, rehospitalizations at other institutions at other institutions could not be captured in this study. However, UK is one of 2 centers in the state equipped with staff trained to care for patients with LVADs; and, therefore, the LVAD coordinators arrange for almost all patients requiring hospital admission to be transferred to UK hospital. Therefore, few rehospitalizations likely went uncaptured, and uncaptured hospitalizations were unlikely to differ between frail and non-frail groups.

Conclusion

Many patients with advanced heart failure who undergo LVAD implant are frail preoperatively. The results of this project revealed that preoperative frailty, as determined by 6-MWT <200 m or SPPB ≤ 7/12, was associated with worse postoperative outcomes. Patients determined to be frail by these measures had significantly higher 1-year mortality, longer LOS, longer time mechanically ventilated, increased need for tracheostomy placement, and were more likely to be discharged to an inpatient facility rather than to home. After adjustment for age, gender, BMI, previous sternotomy, and other comorbidities, SPPB ≤ 7/12, remained a significant predictor of these outcomes, highlighting its likely superiority over 6-MWT in defining frailty in this population.

As frailty is associated with negative outcomes, preoperative frailty assessment can help identify patients who many not be good candidates to benefit from LVAD placement or those who may require more resources, closer follow-up, and more aggressive rehabilitation postoperatively. Insights attained from frailty assessment may also be useful in informing patients of more personalized risks associated with their level of frailty as they consider whether to undergo device implantation.

Future research is still needed on the effects of frailty on outcomes after LVAD implant. Reproduction of a study similar to this one at other institutions would likely be beneficial to further confirm and increase the generalizability of the results found here. Additionally, further research is needed to determine which frailty assessment is the best predictor of outcomes in patients undergoing LVAD implantation, whether frailty can be reversed in heart failure patients prior to or after surgery and how this influences outcomes, and frailty’s influence on the change in patients’ quality of life after implantation.

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Table 1. Literature review: Effect of preoperative frailty on outcomes after LVAD implant

Citation	Design	Sample	Frailty Measure	Level of Evidence*	Inpatient mortality	Long term Mortality	LOS	ICU LOS	Time Mech. Ventilated	Non-home discharge	Readmits	QOL
Chung et al. (2014)	Prospective Observational	**n = 72** (16 frail)	**Handgrip strength**	Level III		↑ SS						
Cooper et al. (2017)	Retrospective	**n = 2469** (227 frail)	**Provider score; gait speed**	Level III	↑ NS	↑ SS	Ø				Ø	
Dunlay et al. (2014)	Prospective Observational	**n = 99** (34 frail)	**Frailty deficit index**	Level III		↑ SS	Ø			↑ NS	Ø	
Herberton et al. (2016)	Retrospective	**n = 100** (32 frail)	**Psoas muscle mass**	Level III	↑ NS		↑ NS					
Jha et al (2017)	Retrospective	**n = 40** (19 frail)	**Fried Score**	Level III		↑ NS	↑ SS	↑ SS	Ø			
Joseph et al. (2017)	Prospective Observational	**n = 75** (44 frail)	**Fried Score**	Level III	↑ NS	Ø	↑ SS		↑ SS			
Manghelli et al. (2014)	Prospective observational	**n = 45** (31 frail)	**Fried score**	Level III	↑ NS		↑ NS		↑ SS			
Reeves et al. (2016)	Prospective Observational	**n = 69** (54 frail)	**Fried score**	Level III			↑ NS					↓ SS
Stein et al. (2019)	Prospective Observational	**n = 44**	**Fried score; grip strength**	Level III		↑ SS	↑ SS					
Uzam et al. (2019)	Prospective Observational	**n = 52** (29 frail)	**Fried score**	Level III	↑ NS		↑ NS					

Legend: ↑ = Increase in outcome; ↓ = Decrease in outcome; **Ø** = No change; **SS** = Statistically Significant; **NS**- Not statistically significant

*John Hopkins Levels of Evidence: Level I: Experimental study, RCT; Level II: Quasi Experimental study; Level III: Non-experimental study; Level IV: Opinion of respected authorities, practice guidelines; Level V: Quality improvement projects and case reports (John Hopkins University, 2017)

Table 2. Baseline health data for frail and non-frail groups for each frailty cutoff measure

Variable	Overall % (n)	SPPB > 7 Non-frail % (n)	SPPB ≤ 7 Frail % (n)	P value	6 MWT ≥ 200 Non-frail % (n)	6 MWT < 200 Frail % (n)	P value
Age							
19-39	17.5 (21)	19.7 (13)	15.2 (7)	0.340	25.0 (14)	10.9 (7)	0.203
40-59	40.8 (49)	42.4 (28)	39.1 (18)		37.5 (20)	45.3 (29)	
60-79	40.8 (49)	37.9 (25)	43.5 (20)		39.3 (22)	42.2 (27)	
80+	0.8 (1)	0.0 (0)	2.2 (1)		0.0 (0)	1.6 (1)	
Race							
White	90.0 (108)	89.4 (59)	89.1 (41)	1.000	91.1 (51)	89.1 (57)	0.151
Black	10.0 (12)	10.6 (7)	10.9 (5)		8.9 (5)	10.9 (7)	
Gender							
Male	84.2 (101)	83.3 (55)	84.8 (39)	0.837	89.3 (50)	79.7 (51)	0.151
Female	15.8 (19)	16.7 (11)	15.2 (7)		10.7 (6)	20.3 (13)	
BMI							
18.5-24.9	21.7 (26)	25.8 (17)	17.4 (8)	0.281	21.4 (12)	21.9 (14)	0.488
25-29.9	22.5 (27)	25.8 (17)	21.7 (10)		26.8 (15)	18.8 (12)	
30-39.9	45.0 (54)	36.4 (24)	50.0 (23)		42.9 (24)	46.9 (30)	
>40	10.8 (13)	12.1 (8)	10.9 (5)		8.9 (5)	12.5 (8)	
EF							
<20%	84.0 (100)	86.2 (56)	80.4 (37)	0.421	89.1 (49)	79.7 (51)	0.163
≥20%	16.0 (19)	13.8 (9)	19.6 (9)		10.9 (6)	20.3 (13)	
CM type							
Non-ischemic	50.8 (61)	51.5 (34)	47.8 (22)	0.701	55.4 (31)	46.9 (30)	0.345
Ischemic	49.2 (59)	48.5 (32)	52.2 (24)		44.6 (25)	53.1(34)	
HF class							
3c	5.0 (6)	7.6 (5)	2.2 (1)	0.035	5.4 (3)	4.7 (3)	0.148
3d	14.2 (17)	16.7 (11)	6.5 (3)		19.6 (11)	9.4 (6)	
4d	80.8 (97)	75.8 (50)	91.3 (42)		75.0 (42)	85.9 (55)	
Prior sternotomy							
Yes	20.8 (25)	22.7 (15)	19.6 (9)	0.688	19.6 (11)	21.9 (14)	0.746
No	79.2 (95)	77.3 (51)	80.4 (37)		80.4 (45)	78.1 (50)	
DM							
Yes	52.5 (63)	45.5 (30)	56.5 (26)	0.249	41.1 (23)	62.5 (40)	0.019
No	47.5 (57)	54.5 (36)	43.5 (20)		58.9 (33)	37.5 (24)	
COPD							

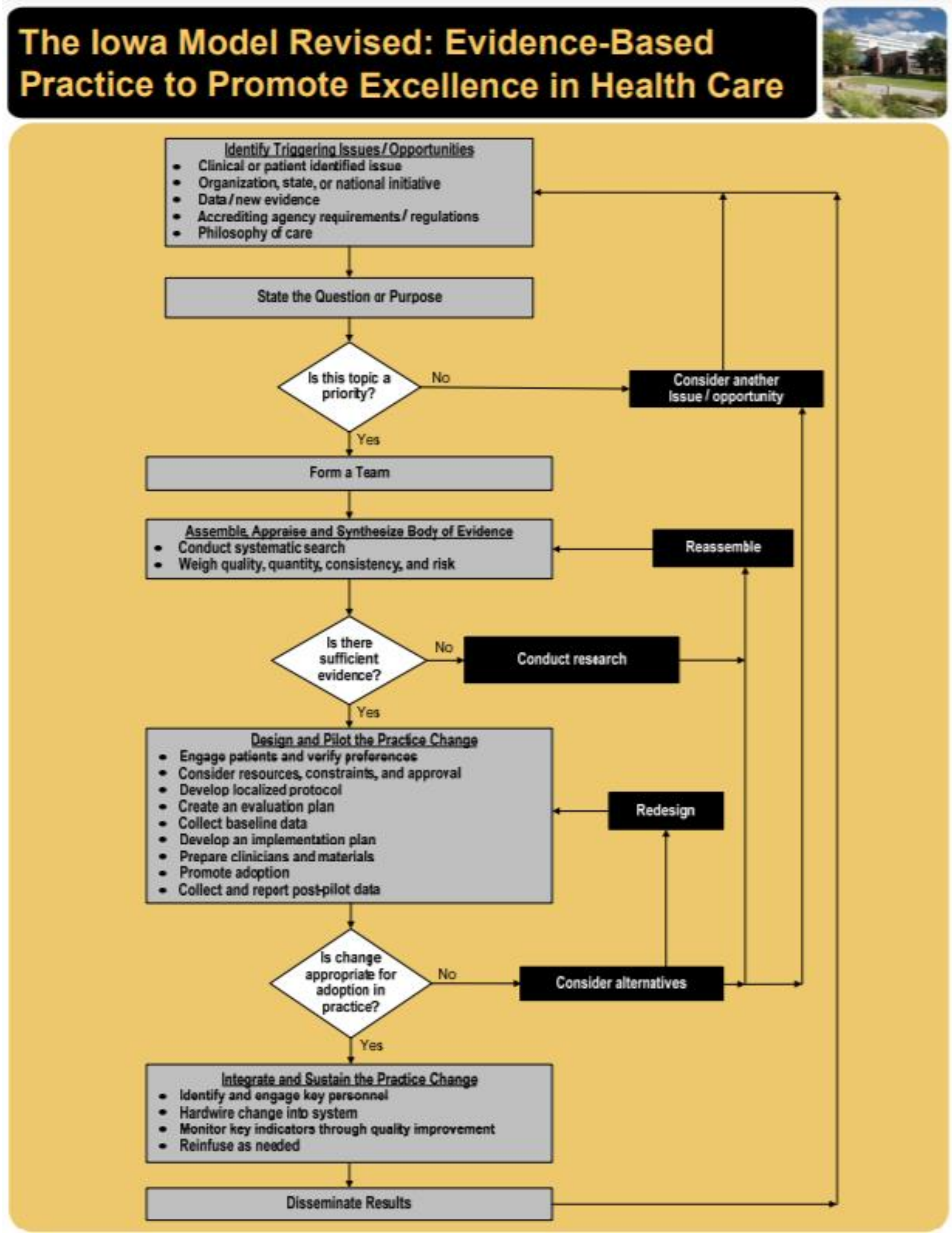
Yes	29.2 (35)	31.8 (21)	23.9 (11)	0.362	28.6 (16)	29.7 (19)	0.893
No	70.8 (85)	68.2 (45)	76.1 (35)		71.4 (40)	70.3 (45)	
HTN							
Yes	65.0 (78)	65.2 (43)	60.9 (28)	0.644	69.6 (16)	60.9 (39)	0.319
No	35.0 (42)	34.8 (23)	39.1 (18)		30.4 (17)	39.1 (25)	
CKD							
Yes	44.2 (53)	43.9 (29)	39.1 (18)	0.612	46.4 (26)	42.2 (27)	0.641
No	55.8 (67)	56.1 (37)	60.9 (28)		53.6 (30)	57.8 (37)	
Pulm HTN							
Yes	39.2 (47)	34.8 (23)	43.4 (20)	0.356	33.9 (19)	43.8 (28)	0.272
No	60.8 (73)	65.2 (43)	56.5 (26)		66.1 (37)	56.3 (36)	
RVEF reduction							
normal	16.1 (19)	20.3 (13)	10.9 (5)	0.277	14.5 (8)	17.5 (11)	0.711
mild	20.3 (24)	18.8 (12)	21.7 (10)		23.6 (13)	17.5 (11)	
mild/mod	9.3 (11)	9.4 (6)	8.7 (4)		5.5 (3)	12.7 (8)	
mod	23.7 (28)	25.0 (16)	21.7 (10)		30.9 (17)	17.5 (11)	
mod/severe	12.7 (15)	10.9 (7)	15.2 (7)		10.9 (6)	14.3 (9)	
severe	17.8 (21)	15.6 (10)	21.7 (10)		14.5 (8)	20.6 (13)	
LVAD type							
HVAD	51.7 (64)	48.5 (32)	63.0 (29)	0.340	50.0 (28)	53.1 (34)	0.873
HMII	18 (15)	10.6 (7)	8.7 (4)		14.3 (8)	15.6 (10)	
HM3	33.3 (40)	40.9 (27)	28.3 (13)		35.7 (20)	31.3 (20)	
INTERMACS							
1	5.9 (18)	7.9 (5)	23.8 (10)	0.080	7.5 (4)	23.3 (14)	0.123
2	41.6 (47)	49.2 (27)	40.5 (17)		45.3 (24)	38.3 (23)	
3	39.8 (45)	47.6 (30)	31.0 (13)		45.3 (24)	35.0 (21)	
4	2.7 (3)	1.6 (1)	4.8 (2)		1.9 (1)	3.3 (2)	

Table 3. Outcomes of frail and non-frail groups for each cutoff measure

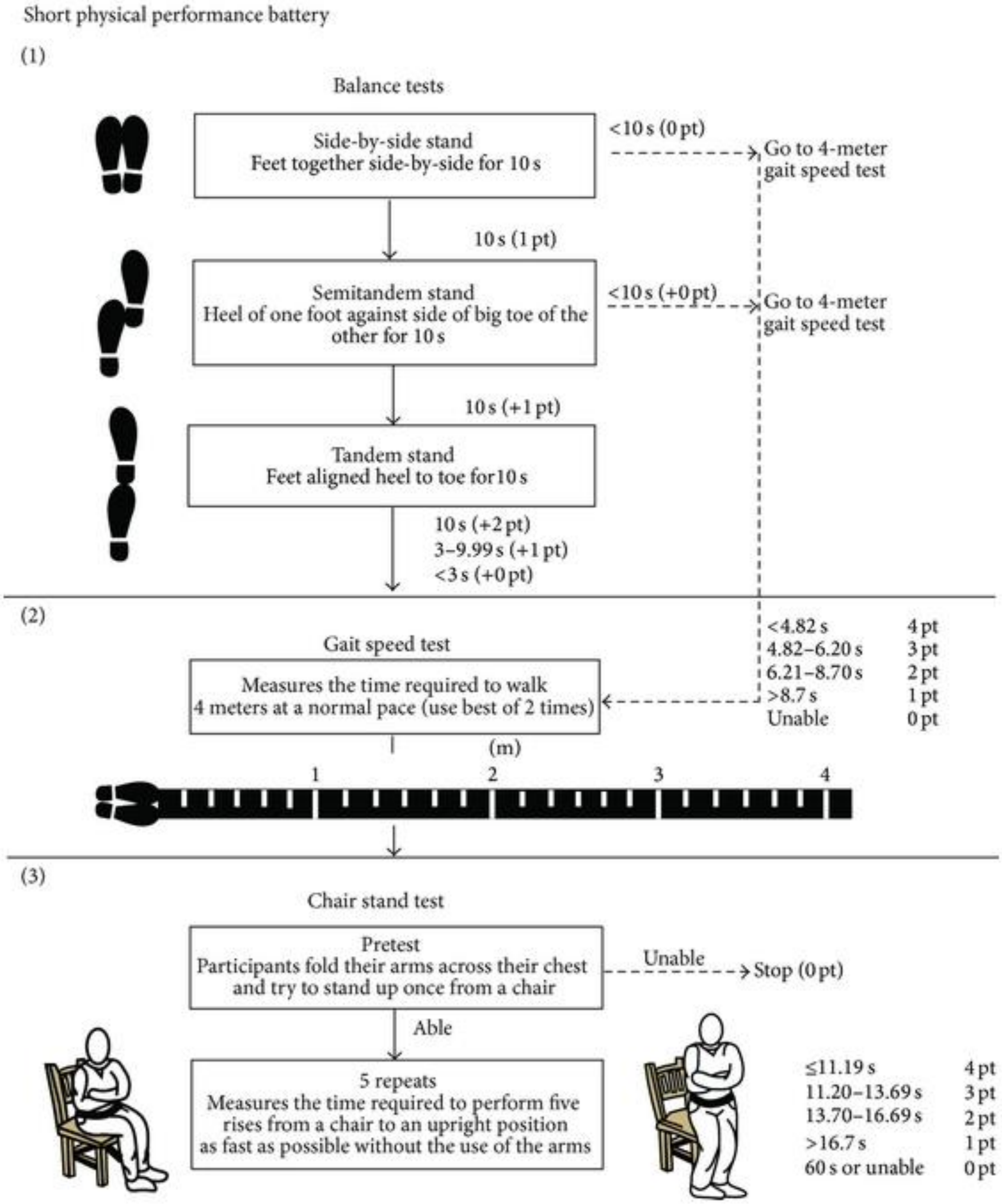
Outcome	SPPB ≤ 7 Frail (n=46)	SPPB > 7 Non-frail (n=66)	P value	6 MWT < 200 Frail (n=64)	6 MWT ≥ 200 Non-frail (n=56)	P value
1-year mortality	33.3% (15)	15.6% (10)	0.030	31.3% (20)	13.2% (7)	0.021
Inpatient mortality	13.0% (6)	9.1% (6)	0.546	10.9% (7)	9.8% (5)	0.714
Hospital LOS (days)*	31 [21,45]	18.5 [15,26]	<0.001	24 [17.25,43]	19 [15,26]	0.012
ICU LOS (days)*	15 [11,34]	9.5 [7,13.75]	<0.001	13 [8,21.75]	10 [7,13]	0.059
Hours Mechanically ventilated*	81 [23,308]	22.75 [18.5,60.63]	<0.001	71.25 [22.63, 136.25]	22 [17,50.5]	<0.001
Tracheostomy placement	31.1% (14)	4.6% (3)	<0.001	23.8% (15)	5.5% (3)	0.006
Discharge to inpatient facility	55.0% (22)	16.7% (10)	<0.001	47.4% (27)	11.8% (6)	<0.001
30-day readmission	20.0% (8)	18.6% (11)	0.886	25.0% (14)	17.6% (9)	0.355
90-day readmission	40.0% (16)	37.3% (22)	0.785	41.1% (23)	41.2% (21)	0.991
Mean change in EQ-5D-3L score (points)	+4.8	+4.1	0.751	+4.88	+3.83	0.439
Mean change in KCCQ-12 scores (points)	+15.8	+11.0	0.371	+17.67	+11.6	0.206

*LOS, ICU LOS, and hours mechanically ventilated are expressed as median [interquartile range]

Appendix A: Iowa Model Flow Chart



Appendix B: Short Physical Performance Battery



Note: The SPPB was developed by the National Institute on Aging in the United States and is available for use without permission or royalty fees.

Image retrieved from Bogin et al., 2014.

Appendix C: Study Variables with Measures

Variable	Measure
Preoperative Frailty measures	
Frailty determined by six-minute walk time (6-MWT)	<200 m walked during 6 MWT (Y/N)
Frailty determined by short physical performance battery (SPPB) score	SPPB score ≤7/12 (Y/N)
Postoperative Outcomes Measures	
Postoperative hospital length of stay (LOS)	Days
Postoperative ICU LOS	Days
Time on mechanical ventilation	Hours
Placement of tracheostomy	Documented tracheostomy operative note (Y/N)
Discharge disposition	Type of location documented in discharge note (i.e. home, rehabilitation facility, long term care facility)
Inpatient mortality	Documented time of death during operative admission (y/n)
1-year mortality	Documented death during 1st postoperative year (y/n)
Readmission at **-30 days** **-90 days**	Documented hospital readmission at - 30 days (y/n) - 90 days (y/n) of discharge after LVAD implantation
Change in quality of life (QOL) scores	Numerical change in pre/postop EQ-5D-3L* quality of life score Numerical change in pre/postop KCCQ-12** Score
Variable	**Measure**
Postoperative Frailty Measure	
Postoperative frailty on 6 MTW	<200 m walked during 6-MWT (Y/N)
Demographic and Baseline Heath Measures	
Age at time of implant	Years: 19-39 40-59 60-70 80+
Gender	Male/Female
Race	White African American Other

Ejection Fraction	≥20% <20%
New York Heart Failure (NYHF) Classification/ American Heart Association (AHA) Stage	Class IIIc, IIId, or IVd
Body Mass Index (BMI)	<18.5 k/m^2 18.5-24.9 k/m^2 25 – 29.9 k/m^2 30-39 k/m^2 >40 k/m^2
Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profile score	INTERMACS profile 1-6
Cardiac Index	L/min/m2
Pre-implant reduction in right ventricular ejection fraction (RVEF)	Normal Mild Mild-Moderate Moderate Moderate to Severe Severe
Comorbid presence of diabetes (DM)	Documented diagnosis of DM (Y/N)
Comorbid presence of hypertension (HTN)	Documented diagnosis of HTN (Y/N)
Comorbid presence of chronic kidney disease (CKD)	Documented diagnosis of CKD (Y/N)
Comorbid presence Chronic obstructive pulmonary disease (COPD)	Documented diagnosis of COPD (Y/N)
Diagnosed pulmonary hypertension	Documented diagnosis of pulmonary HTN (Y/N)
Type of LVAD implanted	HVAD Heartmate II Heartmate 3
Ischemic vs non-ischemic cardiomyopathy	Documentation either ischemic or non-ischemic cardiomyopathy
Prior sternotomy	Documentation of prior sternotomy (y/n)

*3-level EuroQol 5 Dimensions Questionnaire (EQ-5D-3L)

**12-item Kansas City Cardiomyopathy Questionnaire (KCCQ-12)